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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/696,042	10/25/2000	Shiyu Li	44908-00005	4438

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Alan R Thiele
Jenkins & Gilchrist, P.C.
1445 Ross Avenue, Suite 3200
Dallas, TX 75202-2799

EXAMINER

HAAS, WENDY C

ART UNIT

PAPER NUMBER

1661

DATE MAILED: 07/01/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/696,042

Applicant(s)

LI, SHIYOU

Examiner

Wendy C Haas

Art Unit

1661

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 March 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-47 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-47 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: |

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DETAILED ACTION

The amendment for reconsideration has been received and entered March 31, 2003. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office action.

Drawings

This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

Specification

Claim Rejections - 35 USC § 112

Claims 1, 2, 14, 15, 27 and 28 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the reasons stated in the first Office Action. Applicant's arguments have been considered but are not found to be persuasive for the following reasons:

Applicant asserts that the specification provides guidance on how all plant hormones control CPT production because it states "Three plant hormones (auxins, cytokinins and gibberellins) are known to promote and regulate the growth of a plant, and two plant hormones (abscisic acid and ethylene) are known to either inhibit plant growth or promote plant growth to maturity." The Examiner disagrees with applicant's assertion and believes this statement provides only a general overview of how some plant hormones may affect plant tissues in general.

Applicant asserts that Example 3 in the specification illustrates the formation of CPT by ABA accumulation due to water stress. Applicant has provided no clear indication that the water stress the plant was subjected to specifically raised ABA levels in the plant studied. In a complex physiological system such as a plant it is impossible to assume in the absence of clear scientific proof that the effect of a noted stressor would be upon only one hormonal method of regulation, such as ABA. Further, Fig. 21(a), which illustrates the results of Example 3, indicates that there is no statistically significant difference in CPT yield between plants subjected to natural dry conditions and irrigated plants.

Applicant further argues that the art is unpredictable because CPT yields in Vincent et al. vary. The examiner acknowledged the unpredictability of the physiological art in the first Office action and noted that the applicants have disclosed a working method for controlling **auxin** levels only.

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Claims 8, 21 and 34 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, each of the amended claims states "heading back stems with a crotch angle less than about 30 degrees from the main stem of the plant to about 50 cm. above the ground." As noted in the first Office Action, applicant appears to advocate cutting branches that come off of a main leader to the ground. This is impossible. Branches that come off a main leader can only be cut back to the point of origin. Correction and / or clarification regarding the intended meaning of these claims is still needed.

Claim Rejections - 35 USC § 102

Claims 1-3, 4-6, 27-29, 40-41, 43, 46 and 47 remain rejected under 35 U.S.C. 102(b) as being clearly anticipated by Vincent et al. [IDS reference # C-49] taken in view of Li et al. [IDS reference # C-1] and Liu [IDS reference # C-34] for the reasons stated in the first Office Action. Applicant's arguments have been considered but are not found to be persuasive for the following reasons:

Applicant states "simply knowing that trichome or alkaloids are involved in plant defense does not make the method to induce the alkaloids obvious." Rejections under 35 USC § 102(b) are not based on whether or not the method is obvious. The rejection is made merely because the method has been **disclosed in the prior art more than one year prior to this application for patent.**

Applicant argues that alkaloids only accumulate at certain stages and are then transported to other sites in the plant. The Examiner disagrees with this assertion because the prior art shows that CPT is formed in glandular leaf trichomes and is stored within their vacuoles.

Applicant argues past experiments showed contradictory results as to the level of CPT concentration in young leaves. The Examiner does not believe this argument is relevant because the prior art shows that by 1995, more than one year prior to the filing date of this application for patent, it was known that young leaves contain useable concentrations of CPT. Any uncertainty in the art prior to that time is irrelevant. In fact, Vincent et al. state they were motivated to design their experiment "[b]ecause camptothecin accumulates in young leaves," and further state "young leaves contain the highest concentration of CPT in the tree."

Applicant argues that Vincent et al. do not teach that pruning can induce leaf biomass growth over non-pruning. The Examiner notes that the concept of leaf biomass increasing with pruning is very well known in the art, as evidenced by the numerous references cited by the Examiner in the first Office Action Rejections under 35 U.S.C. 103(a). A person of ordinary skill in the art at the time the invention was made would know that pruning a woody plant will increase its leaf biomass.

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Applicant argues that Vincent et al. achieved less than 6% of the CPT yield achieved by the present invention and that Vincent et al. produced only 14.6 mg of CPT in 6 weeks. This statement is incorrect. Vincent et al. produced 175 mg of CPT in six weeks. Applicant asserts that their production of 247 mg of CPT is 16 times the production of Vincent et al. Fig. 24(b) indicates that in a six week period applicant produced 80 mg of CPT. The Examiner notes that the claims recite only an increase in CPT production, not a quantifiable increase. Furthermore, a direct correlation of overall CPT yield between applicant's method and Vincent et al. is difficult because applicant's trees were grown for an unknown period of time and pruned four times over a 11 1/2 month time period. During this time, the plants were never allowed to attain a height of more than 50-60 cm. It is clear from applicant's disclosure that the plants had a shrub-like appearance and greater leaf mass. In contrast, Vincent et al. grew their plants for 17 months to a height of 1.5 m and then pruned them one time, then once more. These plants would have a more tree-like appearance and fewer leaves. Applicant's data came from the best 5 of 69 plants while Vincent et al. collected their data from the 6 plants they had. Applicant was free to select better-than-average performers, while Vincent et al. were limited to the plants they had, including one noted unusually poor performer. Finally, Vincent et al. report a production of 15 mg CPT per gram of dry weight, while applicant reports in terms of fresh weight. It is impossible to correlate a dry weight and a fresh weight determination as it is not possible to know how much water any individual plant tissue is holding. For these reasons, the Examiner is unconvinced that applicant's method shows any patentable distinction over Vincent et al., another known pruning method that increases CPT production.

Applicant argues that people of ordinary skill in the art will assume that trichome density is not affected by pruning because trichomes are not mentioned by either Vincent et al. or Liu et al. The Examiner finds this argument unpersuasive for two reasons. First, if increased CPT production from pruning is a result of increased trichome density, then this physiological event occurs whenever the plant is pruned, whether it is specifically mentioned or not. Second, a prudent person of ordinary skill in the art would make no assumption whatsoever regarding trichomes where they are not mentioned at all.

Applicant argues that IDS reference #c-1 makes no mention of trichomes. This statement is correct. The Examiner notes, however that no motivation is needed for a rejection under 35 U.S.C. § 102(b); the references cited by Li et al. and Liu et al. are mentioned merely as extrinsic evidence of what was known to a person of ordinary skill in the art at the time the invention was made. Further, IDS reference #C-1 notes (page 42) that leaves have the highest concentration of CPT in the tree.

Claim Rejections - 35 USC § 103

Claims 1-6, 8, 10-12, 14-19, 21, 23-25, 27-32, 34 and 36-38 remain rejected under 35 U.S.C. 103(a) for the reasons set forth in the first Office Action. Applicants arguments have been considered and are not found to be persuasive for the following reasons:

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Applicant argues that the prior art teaches away from the claimed invention because the topping of large trees is discouraged. The Examiner notes that the topping of a large tree differs significantly from topping a tree of a large tree species when the individual specimen is under a meter tall. Deciduous tree species are rarely harvested for their foliage. Rather, they are normally grown as specimens. In short, the prior art would not apply because it is not directed towards a small plant.

Applicant further argues that inconsistent findings in the past would teach away from utilizing young leaves as a source of CPT, noting in Table 1 that findings historically have differed. The Examiner finds this argument unpersuasive because there is nothing in Table 1 to indicate that leaves would be an inappropriate source of CPT and leaves are the most readily regenerable biomass of the structures examined.

Applicant argues that Vincent et al., Liu et al., and Li and Adair do not increase CPT yield because the % CPT concentration remains relatively stable. The Examiner notes that these references do illustrate an overall increase of CPT, presumably based on at least increased biomass (Vincent et al. show increased biomass production in 6 week treatments.) The Examiner finds applicant's argument particularly unpersuasive because Fig. 15 of this disclosure notes that the pruned plant demonstrates a lower % of CPT than the unpruned control and Fig. 17(b) similarly shows that pinching correlates to a % fresh weight decrease in CPT production. The data from these figures would also appear to indicate that the increased CPT production **may** be attributable primarily to increased biomass.

Applicant argues that Liu et al. fail to teach that coppiced shoots have a higher CPT concentration than not coppiced shoots. The Examiner notes that plants that are coppiced have **more** shoots and will therefore produce more CPT.

Claims 7, 20 and 33 remain rejected under 35 U.S.C. 103(a) for the reasons stated in the first Office Action.

Applicant argues that Cook teaches root pruning only for shrubs. The Examiner notes that shrubs are also woody plants and that root pruning is utilized for size control in tree species of woody plants as well, such as in bonsai.

Applicant further argues that the teachings of Baldwin do not apply because tobacco is herbaceous and nicotine is synthesized via a differing biosynthetic pathway. The Examiner cites Baldwin as an example of the hormonal effect of root pruning on auxin and/or ABA production and transport in plants; this would apply to any plant.

Claims 13 and 26 remain rejected under 35 U.S.C. 103(a) for the reasons set forth in the first Office Action.

Claims 22 and 35 remain rejected under 35 U.S.C. 103(a) for the reasons set forth in the first Office Action.

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Applicant argues that Baldwin does not teach any pinching techniques. The Examiner believes that any method of removing a portion of a leaf qualifies as "pinching" and notes, at any rate that Baldwin (Oecologia) clearly demonstrates "pinching" of the kind that matches applicants perception of how the term should be interpreted.

Claims 43 and 44 remain rejected under 35 U.S.C. 103(a) for the reasons set forth in the first Office Action.

Applicant argues that sonification would not break trichome walls because they are thicker. The Examiner disagrees. There is no evidence that van Hengel's method did not break trichome cell walls along with the other cell walls broken and in the absence of clear evidence to the contrary a person of ordinary skill in the art could expect all plant cell walls to be broken by van Hengel's method, even the nominally thicker cell walls of trichomes.

Claim 43 and 45 remain rejected under 35 U.S.C. 103(a) for the reasons set forth in the first Office Action.

Applicant argues that without knowledge of trichomes as the CPT accumulation site there would be no motivation to use a homogenizer as a method of breaking cell walls. The Examiner finds this to be unpersuasive. A homogenizer is an efficient way to break cell walls and cell walls would need to be broken to extract the chemical constituents of a leaf, regardless of their location.

Claim 42 is rejected under 35 U.S.C. 103(a) as being unpatentable over Vincent et al. The teachings of Vincent et al. are set forth above. Vincent et al. do not teach the use of fresh, rather than freeze-dried starting material.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use fresh rather than freeze-dried material in order to decrease the amount of trichomes falling away from a leaf harvested from a plant. The **motivation** for this combination is that the faster you process the leaf, the less the leaf will degenerate. Thus, the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

No claim is allowed.

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Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

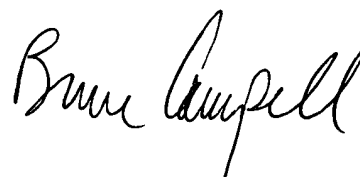
Future Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Wendy C. Haas whose telephone number is (703) 308-8898. The Examiner is normally available Monday through Friday from 9 a.m. to 5:30 p.m.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Bruce Campell, can be reached on (703) 308-4205. The fax number for the group is (703) 305-3041 or (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Matrix Customer Service Center whose telephone number is (703) 308-0196.

W.C. Haas



**BRUCE R. CAMPELL, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600**